MARKED-UP VERSION OF AMENDMENTS:

Specification Amendments Under 37 C.F.R. § 1.121(b)(1)(iii)

Please insert the following paragraph at page 1, between lines 1 and 2, with the following paragraph:

RELATED APPLICATIONS

This Application is a continuation-in-part of International Application No. PCT/GB00/02848, filed on July 24, 2000 and also claims the benefit of U.S. Provisional Application No. 60/146,556, filed on July 30, 2000 and UK Application No. GB9917416.1, filed on July 23, 1999. The entire teachings of the above applications are incorporated herein by reference.

Please replace the paragraph at page 24, lines 16 through 25, with the paragraph below, which is marked up by way of bracketing and underlining to show the changes relative to the previous version of the paragraph:

Exogenously added HIV-1-trans-activating protein (Tat) can translocate through the plasma membrane and to reach the nucleus to transactivate the viral genome. Translocational activity has been identified in amino acids 37-72 (Fawell et al., 1994, *Proc. Natl. Acad. Sci. U. S. A.* 91, 664-668), 37-62 (Anderson et al., 1993, *Biochem. Biophys. Res. Commun.* 194, 876-884) and 49-58 (having the basic sequence RKKRRQRRR (SEQ ID NO:1)) of HIV-Tat. Vives, et al. (1997), *J Biol Chem* 272, 16010-7 identified a sequence consisting of amino acids 48-60 (CGRKKRRQRRRPPQC (SEQ ID NO:2)), which appears to be important for translocation, nuclear localization and trans-activation of cellular genes. Intraperitoneal injection of a fusion protein consisting of β-galactosidase and a HIV-TAT protein transduction domain results in delivery of the biologically

active fusion protein to all tissues in mice (*Schwarze* et al., 1999, Science 285, 1569-72).

Please replace the paragraph starting on page 24, line 26 through page 25, line 11, with the paragraph below, which is marked up by way of bracketing and underlining to show the changes relative to the previous version of the paragraph:

The third helix of the *Drosophila* Antennapedia homeodomain protein has also been shown to possess similar properties (reviewed in Prochiantz, A., 1999, *Ann N Y Acad Sci*, 886, 172-9). The domain responsible for translocation in Antennapedia has been localized to a 16 amino acid long peptide rich in basic amino acids having the sequence RQIKIWFQNRRMKWKK (SEQ ID NO:3); (Derossi, et al., 1994, *J Biol Chem*, 269, 10444-50). This peptide has been used to direct biologically active substances to the cytoplasm and nucleus of cells in culture (Theodore, et al., 1995, *J. Neurosci* 15, 7158-7167). Cell internalization of the third helix of the Antennapedia homeodomain appears to be receptor-independent, and it has been suggested that the translocation process involves direct interactions with membrane phospholipids (Derossi et al., 1996, J Biol Chem, 271, 18188-93). The VP22 tegument protein of herpes simplex virus is capable of intercellular transport, in which VP22 protein expressed in a subpopulation of cells spreads to other cells in the population (Elliot and O'Hare, 1997, *Cell* 88, 223-33). Fusion proteins consisting of GFP (Elliott and O'Hare, 1999, *Gene Ther* 6, 149-51), thymidine kinase protein (Dilber et al., 1999, *Gene Ther* 6, 12-21) or p53 (Phelan et al., 1998, *Nat Biotechnol* 16, 440-3) with VP22 have been targeted to cells in this manner.